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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,469	04/20/2001	William D. Huse	P-IX 4692	2981

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EXAMINER	
BAKER, MAURIE GARCIA	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/839,469	HUSE ET AL.	
	Examiner	Art Unit	
	Maurie G. Baker	1639	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 February 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *12 February 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☒ The proposed amendment(s) will not be entered because:

(a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☒ they raise the issue of new matter (see Note below);

(c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☒ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: *Please see attached.*.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *Please see attached*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1-9*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

MAURIE GARCIA BAKER PH.D
PRIMARY EXAMINER

ADVISORY ACTION

Attachment

1. Applicant's After Final amendment filed February 12, 2004 raises new issues which would require further search and/or consideration and does not place the case in better form for appeal or in condition for allowance. Moreover, the proposed amendment appears to contain new matter. Thus the amendment will *not be entered*.

2. Applicant proposes to add the phrase "relative to a parent receptor of said receptor variant population" to claim 5. This appears to be *new matter*. The After Final amendment filed February 12, 2004 does not point to any specific support for the newly proposed claim language.

3. Also, Applicant proposes to add several new claims (proposed claims 39-47) and does not cancel any finally rejected claims. This is improper. See MPEP 714.13.

4. Applicant's arguments are moot in view of the non-entry of the amendment. Due to the non-entry of the amendment, all previous rejections are maintained for reasons of record. However, in the interest of compact prosecution, the following is noted.

5. Applicant points out that claims 6 and 7 recite recombinant expression of the receptor variant population, not the ligands. This is noted and is a correct statement of the claim's recitations; the statement in the Office Action referring to ligands was a typographical error.

6. Applicant argues that the claims are adequately described and refers to the specification and prior art for support. However, the examiner's position is that the "collective receptor variant population" recited in the claims could encompass a virtually unlimited number of compounds. This is because the instant claims give ***no structure*** for

the receptor itself and no structural information as to the specific "variant". Thus the claims could encompass an infinite number of variations. As also stated in the rejection, the examiner pointed out that the specification discloses only very limited and mostly prophetic examples of carrying out the claimed method. While an example is indeed not required, lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art. One of ordinary skill would not necessarily expect to be able to extrapolate the disclosed specific example (i.e. Example V) as far as its applicability to the instant generic claims. Moreover, when there is little to no disclosure in the instant specification of the starting material or conditions under which claimed process can be carried out, this failure cannot be rectified by asserting that all disclosure related to the process is within skill of art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997).

7. Again, with respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (cited in previous action) regarding disclosure. For adequate disclosure, like enablement, requires representative examples which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and **University of California v. Eli Lilly and Co cited above (for disclosure)**. The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. A representative number of species means that the species that are adequately described are representative of the entire genus. When there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The examiner's position is that a sufficient variety of species have not been described, as the variation within the genus would be extremely large.

8. Also as stated previously, the examiner deems the art to be unpredictable. The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Additionally, the Board has held on the issue of unpredictability that "... the unpredictability of an art area alone may be enough to create a reasonable doubt as to the accuracy of statements in the specification." *Ex parte Singh*, 17 U.S.P.Q.2d 1714,1716 (B.P.A.I. 1990).

9. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). The examiner maintains because of the breadth of the claims, the unpredictability of the art and the lack of adequate working examples the above standard is not met. Thus, the rejection of claims 1-9 under 35 U.S.C. 112, first paragraph is deemed to be proper and is maintained.

10. With respect to enablement, Applicant argues that the claims are enabled and refers to the instant specification concerning methodology. However, the terms/methods described by applicant are set forth in only the broadest terminology. As stated in the rejection, no limitations on the specific structure of the ligand or receptor are given and, as such, this could read on a wide variety of structures. The invention is such that each of the components must be present in operable form for successful practice of the invention. For example, the ligand must bind the receptor and the binding must be able to be detected.

11. Applicant argues that the art is not unpredictable and cites prior art in support of such. The examiner's position is that the art is indeed unpredictable for the reasons set forth in the rejection. For example, the structures of possible variants are sufficiently diverse that one of ordinary skill would not be able to predict their structures with respect to the linking of the receptor variant to an "identifiable tag". In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved. See *In re Fisher*, 57 CCPA 1099,427 F.2d 833,839,166 USPQ 18,24(1970). Additionally, the Board has held on the issue of unpredictability that "... the unpredictability of an art area alone may be enough to create a reasonable doubt as to the accuracy of statements in the specification." *Ex parte Singh* (cited above).

12. Applicant points to various ligand/receptor pairs taught by the prior art. The instant claims are not limited to such pairs or even to *any* specific pair. The examiner's position is that the instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in making and using the claimed invention. Most importantly, ***the instant specification fails to identify that structure which is required for the claimed activity***. In the absence of such guidance, a practitioner of the art would have to resort to a substantial amount of experimental trial and error to produce a "collective receptor variant population" that has the required functional limitations (i.e. "linked to an identifiable tag"). This trial and error would clearly constitute undue experimentation. Applicant states that limiting the claims to a specific ligand receptor pair would require that the result of the method be known in advance. Limitation to a specific pair is not what is required, but, as stated above, clear knowledge of the ***structure which is required for the claimed activity*** is needed.

13. Applicant also argues that one of ordinary skill would know how to tag the claimed receptors. The examiner respectfully disagrees as such processes were unpredictable and highly dependent on compound structure (as evidenced by the cited

Janda reference). Again, ***no structure*** for the instant "collective receptor variant population" and no working examples of tagging are provided. Thus, the rejection of claims 1 and 9 under 35 U.S.C. 112, first paragraph is deemed to be proper and is maintained.

14. The terminology proposed to be added to claim 5 not only appears to be new matter, but does not obviate the rejection under 35 U.S.C. 112, second paragraph. The claim still recites that the receptor variants have "optimal binding activity". The term "optimal" is a relative term which renders the claim indefinite. Also, the new terminology "relative to a parent receptor of said receptor variant population" is by its very nature, relative as well.

15. Lastly, Applicant argues that Lerner et al does not teach a "collective receptor variant population" stating that "the subject specification teaches the use of a collective receptor variant population and not random cDNA libraries". However, there is nothing in the instant claims or specification that indicates that random cDNA libraries would be excluded from a "collective receptor variant population". Also, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, importantly, the disclosure of random cDNA libraries in Lerner et al is ***not*** the only disclosure of expression of GPC receptors. As pointed out in the rejection, there are many portions of Lerner et al that disclose expression of a multiplicity of receptors. See portion of rejection cited below:

> The method uses expression of the receptors in pigment cells, specifically melanophores (see, for example, column 13, lines 54-67; Example 6 in columns 17-19 and patented claims 9-10). Lerner et al disclose a multiplicity of GPC receptors that are expressed, see, for example, column 14, lines 31-49 and column 15, lines 3-11. The reference clearly teaches "cloning new GPC receptors" (see column 15, lines 17-22; and patented claims 9-10; for example); this reads directly on the claimed "collective receptor variant population".

For these reasons, the rejection under 35 U.S.C. 102(b) is deemed to be proper and is maintained.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (571) 272-0805. The examiner is on an increased flextime schedule; the best time to contact the examiner is Monday-Friday from 6:00-10:00 a.m.

17. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached at (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Maurie Garcia Baker, Ph.D.
March 21, 2004

MAURIE GARCIA BAKER PH.D
PRIMARY EXAMINER